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Stability of Gompertz model parameters with mortality deceleration rate

Mathematics

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ABSTRACT

In the absence of age speci_c mortality data, the stability analysis (with respect to the population size) of the age-dependent parameter in the Gompertz survival model with a mortality deceleration rate leads to conclude the constancy of the parameter

1 Introduction

Aging research has long employed demogaphic models of age-speci_c adult mortality that are based on approximately exponential increase in mortality, the best known being the Gompertz model which has been the major mortal- ty model in gerontology for more than 65 years [1, 2]. In humans and many

orgaisms the mortality rate m(t) increases approximately exponentially with age [3]. Gompertz [4] was the _rst to recognize this dependency of mortality rate on chronological age and expressed it mathematically by

$$m(t) = Ae^{\alpha t}, \tag{1}$$

where m(t) is the mortality rate at time t, the positive parameter A is the age-independent mortality rate or the initial mortality rate and the positive parameter _ is the age-dependent mortality rate. The corresponding survival function can be obtained by integrating the mortality rate given in (1). i.e.,

$$S(t) = e^{\frac{A}{\alpha}(1-e^{\alpha t})} \tag{2}$$

ıor a popuıatıon oı sıze ɴ, tne age at wnıcn tne popuıatıon nas diminished to one survivor is (S(t) = 1/N) approximates tm. Species comparisons in mortality rates are aided by calculations of MRD (mortality rate decrement) which changes in the same direction as lifespan and is given by

$$MRD = \frac{ln2}{\alpha}. \tag{3}$$

In the absence of age-speci_c mortality data, Finch et al.[1] have developed a method to estimate initial mortality rate (IMR) and mortality rate to double (MRD) from the average mortality rate (Aav) and maximum life span (tm).

When studying the physical properties of a problem, it is essential to prove the existence, uniqueness and stability of the problem. M. Pitchaimani and T.Eakin have already proved the uniqueness of age-dependent parameter _ in Gompertz survival model with a mortality deceleration rate [5]. In this work, the stability of the parameter _ with respect to the population size N is established. In view of the mortality deceleration at advanced ages, he stability of Gompertz parameter _ is valid in the Gompertz segment [A, average life span], that is, from puberty to average life span.

2 Estimation of parameters

Trends in human longevity are puzzling, especially when considering the limits of human longevity. It is well known that among most mammals, mor- tality rates are generally lowest at puberty and then accelerate at a constant rate during the major phase of adult life. In human populations, according to published studies (Witten, 1988 [6]), the acceleration of mortality rate slows after 85 years. After 105 years, the mortality rate appears to cease increas- ng and may even decrease at these extremely advanced ages. Decreasing mortality at advanced ages is described in detail for ies ([1]).

There is an additional evidence for the exponential decay at higher age. Quite recently Wang and co-workers disclosed an elegant experiment for the senescence accelerated mouse (SAM), showing that the mouse mortality func- tion also approaches a constant value at higher age (Wang et al.,[7]). All the evidences accumulated so far suggest strongly that the eponential decay of populations at higher age is a general theorem (K.Suematsu et al.,[8]).

In such cases, the Gompertz equation (1) is a poor description of mortality dynamics. To correct for departures from Gompertz, the logistic frailty model was also examined:

$$m(t) = \frac{Ae^{\alpha t}}{1 + s\frac{A}{\alpha}(e^{\alpha t} - 1)}. \tag{4}$$

Early in life (t near zero), mortality increases exponentially at a rate deter- mined by A and _. The parameter s determines the extent to which mortality rates decelerate late in life. Higher values of s indicate greater deceleration. Note that when s = 0, eqn. (4) reduces to eqn.(1). Solving eqn.(4) for MRD

gives

$$MRD = \frac{1}{\alpha} ln\left(\frac{2 - 2sA/\alpha}{1 - 2sA/\alpha}\right). \tag{5}$$

Note that when s = 0, eqn.(5) reduces to eqn.(3).

The corresponding survival function can be obtained by inte-

$$S(t) = \left[1 + s\frac{A}{\alpha}(e^{\alpha t} - 1)\right]^{-\frac{1}{s}}. \tag{6}$$

Choosing t = tmax, the known maximum lifespan, we may set S(tm) = 1/N (the population contains only one individual left from an original population size) for ease of analysis. We obtain the following equation for tm (the time at which the population has only one individual and which approximates the maximum lifespan t*m)

$$t^*_m \simeq t_m = \frac{1}{\alpha} ln\left[1 + \frac{N^s - 1}{s}\frac{\alpha}{A}\right]. \tag{7}$$

The average mortality rate of a steady-state population subject to the age- speci_c mortality rate of eqn.(4) is

$$A_{av} = \frac{1}{\int_0^\infty S(t)dt}. \tag{8}$$

Eqn.(7) gives

$$\frac{A}{\alpha} = \frac{1}{s}\frac{N^s - 1}{e^{\alpha t_m} - 1}, \tag{9}$$

and substituting the value of S(t) into (8), we get

$$\frac{1}{A_{av}} = \int_0^\infty \left(\frac{1}{1 + s\frac{A}{\alpha}(e^{\alpha t_m} - 1)}\right)^{\frac{1}{s}} dt.$$

A simple substitution in the integral gives

$$\alpha = A_{av}\left(\frac{e^{\alpha t_m} - 1}{N^s - 1}\right)^{\frac{1}{s}} \int_{\frac{N^s-1}{e^{\alpha t_m}-1}}^{\infty} \frac{1}{z}\left(\frac{1}{(1+z)\frac{e^{\alpha t_m}-1}{N^s-1} - 1}\right)^{\frac{1}{s}} dz. \tag{10}$$

where $z = s\frac{A}{\alpha}e^{\alpha t}\left(= \frac{N^s-1}{e^{\alpha t_m}-1}e^{\alpha t}\right)$.

The basic equation (10) is transcendental, involving exponential integral and the age-dependent parameter _ is a function of Aav; lnN; tmax. A proof for the theorem on stability of the age dependent parameter is given in the next section.

3 Stability of _ with respect to the population size N

Necessary condition for stability

Let α_1, α_2 be age dependent parameters with population size N_1^s, N_2^s respectively, then

$$\alpha_i = A_{av}\left(\frac{e^{\alpha_i t_m} - 1}{N_i^s - 1}\right)^{\frac{1}{s}} \int_{\frac{N_i^s-1}{e^{\alpha_i t_m}-1}}^{\infty} \frac{1}{z}\left(\frac{1}{(1+z)\frac{e^{\alpha_i t_m}-1}{N_i^s-1} - 1}\right)^{\frac{1}{s}} dz$$

where $i = 1, 2$. Consider

$$\alpha_1 - \alpha_2 = A_{av}\left[\left(\frac{1}{x_1}\right)^{\frac{1}{s}} \int_{x_1}^{\infty} \frac{1}{z}\left(\frac{1}{\frac{1+z}{x_1} - 1}\right)^{\frac{1}{s}} dz - \left(\frac{1}{x_2}\right)^{\frac{1}{s}} \int_{x_2}^{\infty} \frac{1}{z}\left(\frac{1}{\frac{1+z}{x_2} - 1}\right)^{\frac{1}{s}} dz\right]$$

where

$$x_i = \frac{N_i^s - 1}{e^{\alpha_i t_m} - 1}. \tag{11}$$

A simple substitution in the above equation gives

$$\alpha_1 - \alpha_2 = A_{av}(x_2 - x_1)\int_1^\infty \left(\frac{1}{u}\right)^s \frac{1}{(u + x_1 - 1)(u + x_2 - 1)} du.$$

Since $\left(\frac{1}{u}\right)^{\frac{1}{s}} \le 1\ \forall u \ge 1$, we obtain

$$|\alpha_1 - \alpha_2| \le A_{av}|x_2 - x_1| \int_1^\infty \frac{1}{(u + x_1 - 1)(u + x_2 - 1)} du.$$

Set

$$x_1 = \frac{x_1 + x_2}{2} + \frac{x_1 - x_2}{2}, x_2 = \frac{x_1 + x_2}{2} - \frac{x_1 - x_2}{2}. \tag{12}$$

[Note that $\frac{x_1+x_2}{2}$ is the arithmetic mean and $\frac{x_1-x_2}{2}$ is the perturbation term of x_1, x_2].

Substitution of (12) into the above equation results in

$$|\alpha_1 - \alpha_2| \le A_{av}|x_2 - x_1| \int_{\frac{x_1+x_2}{2}}^\infty \frac{1}{(y + \frac{x_1-x_2}{2})(y - \frac{x_1-x_2}{2})} dy,$$

where $y = u - 1 + \frac{x_1+x_2}{2}$.
On the RHS of (12), the expression

$$\frac{1}{\left[y + \frac{x_1-x_2}{2}\right]\left[y - \frac{x_1-x_2}{2}\right]} = \frac{1}{y^2}\left[1 - \frac{x_1 - x_2}{2y} + ...\right]\left[1 + \frac{x_1 - x_2}{2y} + ...\right] \tag{13}$$

can be approximated to $(\frac{1}{y^2})$ by neglecting higher order perturbation terms in each expression on the RHS of (13), since $\left|\frac{x_1-x_2}{x_1+x_2}\right| < 1$.

On account of (13), (12) becomes

$$(\alpha_1 - \alpha_2) = A_{av}|x_1 - x_2| \int_{\frac{x_1+x_2}{2}}^\infty \frac{1}{y^2} dy.$$

Upon integration we get

$$|\alpha_1 - \alpha_2| \le A_{av}\left|\frac{x_1 - x_2}{\frac{x_1+x_2}{2}}\right|. \tag{14}$$

Retrieving x_i from (12) and substituting into equation (14), we get

$$|\alpha_1 - \alpha_2| \le A_{av}\left|\frac{\frac{N_1^s-1}{e^{\alpha_1 t_m}-1} - \frac{N_2^s-1}{e^{\alpha_2 t_m}-1}}{\frac{\frac{N_1^s-1}{e^{\alpha_1 t_m}-1} + \frac{N_2^s-1}{e^{\alpha_2 t_m}-1}}{2}}\right|.$$

Simplifying further, we get

$$|\alpha_1 - \alpha_2| \le A_{av}\left|\frac{N_1^s e^{\alpha_2 t_m} - N_2^s e^{\alpha_1 t_m} + N_2^s - N_1^s + e^{\alpha_1 t_m} - e^{\alpha_2 t_m}}{\frac{N_1^s e^{\alpha_2 t_m} + N_2^s e^{\alpha_1 t_m} - N_2^s - N_1^s - e^{\alpha_1 t_m} - e^{\alpha_2 t_m} + 2}{2}}\right| \tag{15}$$

We represent the age dependent parameter _ as a sum of mean and perturbation as follows:

$$\alpha_1 = \frac{\alpha_1 + \alpha_2}{2} + \frac{\alpha_1 - \alpha_2}{2},\ \alpha_2 = \frac{\alpha_1 + \alpha_2}{2} - \frac{\alpha_1 - \alpha_2}{2}. \tag{16}$$

Substitution of (16) into (15) and after a little algebra we obtain

$$|\alpha_1 - \alpha_2| \le A_{av}\left|\frac{N_1^s P - N_2^s Q + (N_2^s - N_1^s)(e^{-\frac{\alpha_1+\alpha_2}{2}t_m}) + Q - P}{\frac{N_1^s P + N_2^s Q - (N_2^s + N_1^s - 2)(e^{-\frac{\alpha_1+\alpha_2}{2}t_m}) - P - Q}{2}}\right| \tag{17}$$

where we have denoted $P = e^{-\frac{\alpha_1-\alpha_2}{2}t_m}$, $Q = e^{\frac{\alpha_1-\alpha_2}{2}t_m}$.
Since

$$e^{\pm\frac{\alpha_1-\alpha_2}{2}t_m} \approx 1 \pm (\frac{\alpha_1 - \alpha_2}{2})t_m \tag{18}$$

(by neglecting higher order perturbation terms in _1; _2) substituting (18) into equation (17) and simplifying we obtain

$$|\alpha_1 - \alpha_2| \le A_{av}\left|\frac{\frac{N_1^s - N_2^s}{2}\left(1 - e^{-\frac{\alpha_1+\alpha_2}{2}t_m}\right) - (\alpha_1 - \alpha_2)t_m + \frac{(\alpha_1-\alpha_2)t_m}{\frac{N_1^s+N_2^s}{2}}}{\left(1 - e^{-\frac{\alpha_1+\alpha_2}{2}t_m}\right) - 2\frac{\left(1 - e^{-\frac{\alpha_1+\alpha_2}{2}t_m}\right)}{N_1^s+N_2^s} - \left(\frac{\alpha_1-\alpha_2}{2}\right)t_m\left(\frac{N_1^s-N_2^s}{N_1^s+N_2^s}\right)}\right|$$

The last term in the denominator of the above equation is a product of two perturbation terms. We neglect this higher order term to get

$$|\alpha_1 - \alpha_2| \le A_{av}\left|\frac{\frac{N_1^s - N_2^s}{2}\left(1 - e^{-\frac{\alpha_1+\alpha_2}{2}t_m}\right) - (\alpha_1 - \alpha_2)t_m\left(1 - \frac{2}{N_1^s+N_2^s}\right)}{\left(1 - e^{-\frac{\alpha_1+\alpha_2}{2}t_m}\right)\left(1 - \frac{2}{N_1^s+N_2^s}\right)}\right| \tag{19}$$

The above equation takes the form

$$|\alpha_1 - \alpha_2| \le A_{av}\left|\frac{N_1^s - N_2^s}{\frac{N_1^s+N_2^s}{2}\left(1 - \frac{2}{N_1^s+N_2^s}\right)}\right| + A_{av}t_m\left|\frac{\alpha_2 - \alpha_1}{1 - e^{-\frac{\alpha_1+\alpha_2}{2}t_m}}\right| \tag{20}$$

Let

$$\frac{A_{av}t_m}{1-e^{-\frac{\alpha_1+\alpha_2}{2}t_m}} < 1. \qquad (21)$$

Then $0 < e^{-\frac{\alpha_1+\alpha_2}{2}t_m} < 1 - A_{av}t_m$, which is true when $A_{av}t_m < 1$.
If $A_{av}t_m < 1$, further we have

$$-\left(\frac{\alpha_1+\alpha_2}{2}\right)t_m < ln(1-A_{av}t_m)$$

which gives

$$\frac{\alpha_1+\alpha_2}{2} > \frac{1}{t_m} ln\left(\frac{1}{1-A_{av}t_m}\right).$$

Note that the above estimation is independent of the population size N. Clearly, the term $\frac{\alpha_1+\alpha_2}{2}$- mean age dependent parameter.

Theorem 1
The age dependent parameter _ is stable for any population size N, provided
Aavtm < 1 .
Proof
When (21) holds, from (20) we get

$$|\alpha_1 - \alpha_2| \le CA_{av}\left|\frac{N_1^s - N_2^s}{\left(\frac{N_1^s+N_2^s}{2}\right)\left(1-\frac{2}{N_1^s+N_2^s}\right)}\right| \qquad (22)$$

where $C = \frac{1}{1-\left(\frac{A_{av}t_m}{1-e^{-\frac{\alpha_1+\alpha_2}{2}t_m}}\right)} > 0$. Hence it follows from (22) that α is stable for any N.

Remark : There were no recorded samples for $A_{av}t_m < 1$ to compare with (21).

When $A_{av}t_m \ge 1$ (See Table 1), we get

$$\frac{A_{av}t_m}{(1-e^{-\frac{\alpha_1+\alpha_2}{2}t_m})} \ge 1, \qquad (23)$$

since the function $\frac{1}{1-e^{-x}} > 1$ for every positive x and asymptotically goes to

Table 1 (reprinted from [5])

A_{av}	A	α	s	t_m	MRD
Herring gull					
0.34					
N=(652)	0.18	2.2457	0.144	11.3	3.414
N=10^3			0.1509	11.5	3.359
N=10^9			0.0477	15.7	2.974
Human					
0.0154					
N=10^3	0.0002	0.087	0.326	105	7.975
N=10^5			0.182	110	7.972
N=10^7			0.131	114	7.972
N=(80,750,000)			0.110	115	7.972
N=10^9			0.103	117	7.972
N=10^{11}			0.089	120	7.972
Mouse					
0.74					
N=25	0.049	2.567	0.320	2.2	0.272
N=50			0.296	2.3	0.272
N=100			0.180	2.3	0.271
N=(738)			0.172	2.5	0.271
N=10^3			0.151	2.5	0.271
N=10^9			0.043	2.9	0.271
Rat					
0.64					
N=(250)	0.025	.666	0.200	2.6	0.271
N=10^3			0.172	2.7	0.260
N=10^9			0.054	3.1	0.260
Japanese quail					
0.35					
N=(29)	0.091	0.596	0.196	5.8	1.215
N=10^3			0.082	6.9	1.184
N=10^9			0.031	8.8	1.171

Table 2

x	$1/1 - e^{-x}$
0.01	100.501
0.02	50.5017
0.03	33.8358
0.04	25.5033
0.05	20.5042
0.15	7.17916
0.5	2.54149
1.0	1.58198
2.5	1.08943
4.0	1.01866
7.5	1.00055
10.5	1.00003
12.5	1
25	1
52.5	1
70.6	1
100	1

When (23) holds, it follows from (20) that

Theorem 2

The age dependent Gompertz parameter _ to be stable with respect to the

population size N, it is necessary that _ be a constant, that is, MRD = ln2

be a constant.

Remark: Observe that the experimental data given in table 1 con_rms the

theoretical approach of theorem 2.

Corollary :

Since _ is a constant, it is clear that _ is stable also with respect to the

maximum life span tm.

Conclusion:

The age-dependent Gompertz parameter _ is stable when tm is small , oth-

erwise it is necessary that _ be a constant.

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